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Local and serum IgE in vasomotor rhinitis

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SUMMARY

Total and specific IgE in serum and nasal secretions were measured in twenty five subjects with vasomotor rhinitis without asthma (21 perennial vasomotor allergic rhinitis and 4 seasonal vasomotor allergic rhinitis) after Carbacholine nasal challenge-test. The level of total and specific IgE was lower in the pure, non diluted nasal secretions than in the serum. The diagnostic usefullness of these measurements and the concept of "localized allergy" are discussed.

INTRODUCTION

The causes of vasomotor rhinitis linked to pituitary vasomotor dysfunction are diverse. Allergy is one of them. The clinical significance of measurements of total and specific IgE in nasal secretions has not yet been clearly established, despite numerous reports (Deuschl and Johansson, 1977; Houri et al., 1972; Huggins and Brostoff, 1975; Merret et al., 1976; Mygind, 1979; Okuda, 1975). The aim of our study was to measure and compare total and specific IgE both in nasal secretions and in serum in order to assess their theoretical and diagnostic value.

MATERIAL AND METHODS

Our study was performed on thirty two subjects: seven control subjects totally free of any allergic or rhinopharyngeal symptoms, twenty one patients suffering from isolated perennial vasomotor allergic rhinitis and four patients suffering from seasonal vasomotor allergic rhinitis caused by grass pollen. Of the twenty one cases of perennial rhinitis, twelve were definitely allergic to house dust mite and/or animal dander. There was a positive relationship between their clinical-history, skin tests and nasal provocation tests. In nine of the patients the same criteria was inconclusive regarding the cause of their vasomotor rhinitis. It was in this latter group that we held the diagnosis of allergy and a cause might be determined from quantitative determinations of both serum and local IgE.

All of the measurements were carried out concomitantly on all of the patients using the same method. After local stimulation with Carbacholine, nasal secretions were collected in their native, non-diluted state (about 1 ml per nasal fossa).

This test could also be used to explore the parasympathetic component of the vasomotor and secretory (quantitative scale) function or dysfunction of the pituitary. Indeed pituitary dysfunction is the element common to all types of vasomotor rhinitis (Braun, J. J. 1977, 1982; Klotz et al., 1980; Wayoff et al., 1978). Nasal secretions thus collected at the same time as the serum were maintained at −20°C until quantitative determination. After thawing, they were homogenized by adding 50 µl of Tween 20 and by prolonged mixing in a Vortex mixer.

Albumin determination

The quantitative determination of albumin in nasal secretions was performed by Mancini's radial immunodiffusion technic (Behring plate).

Total IgE measurement

The total IgE both locally and in the serum were measured using the PRIST method which was better suited than the RIST method for nasal secretions (Johansson and Deuschl, 1976; Merret et al., 1976).

Specific IgE measurement

For specific IgE, we employed the RAST technic (Phadebas lab.) using the same cord blood as reference (390 CPM Background noise). For all of our quantitative determinations, the specific IgE results from this uniform series are expressed in CPM, PRU and classes 0–4. They were systematically determined for the following allergens: cock's foot (G3). Dermatophagoides pteronyssinus (D1) and house dust (H1). The values above 17.5 PRU were obtained by extrapolation of the reference curve.

Table 1. Serum

rhinitis	case	IgE (UI/ml)	RAST			IgA (mg/l)
				PRU	class 0–4	
NAVR	9	73.83 ± 92.43	D1	0.23 ± 0.10	0.11 ± 0.33	2.64 ± 1.11
			H1	0.17 ± 0.11	0	
PAVR (house dust, mites)	12	551.45 ± 481.43	D1	21.03 ± 22.43	2.58 ± 1.50	2.11 ± 0.73
			H1	10.74 ± 13.13	2.33 ± 1.30	
SAVR (grass pollen)	4	737.33 ± 941.56	G3	35.5 ± 9.61	4	2.56 ± 0.52

NAVR: Non allergic vasomotor rhinitis
PAVR : Perennial allergic vasomotor rhinitis
SAVR : Seasonal allergic vasomotor rhinitis

IgA determination

The local and serum IgA (mg/l) were determined quantitatively by radial immunodiffusion (Tripartigen Behring plate).

RESULTS

Our results are summarized in Tables 1, 2 and 3 (Means, standard deviations). There are large variations in the values observed for levels of albumin, IgE and to a lesser degree for IgA. This variation exists both within each group of rhinitis

Table 2. Nasal secretions

rhinitis	case	IgE (UI/ml)	RAST			IgA (mg/l)	albumin (g/l)
				class 0-4	PRU		
CS	7	N.D.	D1	0.42 ± 0.79	0.28 ± 0.45	N.D.	0.17 ± 0.10
			H1	0	0.17 ± 0.09		
			G3	0	0.22 ± 0.11		
NAVR	9	0.78 ± 0.68	D1	0	0.14 ± 0.05	0.22 ± 0.05	0.54 ± 0.38
			H1	0	0.19 ± 0.07		
PAVR (house dust, mites)	12	11.15 ± 9.92	D1	1.08 ± 1.16	1.81 ± 2.90	0.28 ± 0.25	0.58 ± 0.60
			H1	1.08 ± 0.67	0.64 ± 0.59		
SAVR (grass pollen)	4	44.08 ± 45.43	G3	2.75 ± 0.96	10.56 ± 15.06	0.49 ± 0.59	0.49 ± 0.59

NAVR: Non allergic vasomotor rhinitis
PAVR : Perennial allergic vasomotor rhinitis
SAVR : Seasonal allergic vasomotor rhinitis
CS : Control subjects

Table 3. Comparison between IgE in the nasal secretions (N.S.) and in the serum (S)

rhinitis	case	IgE (UI/ml)		RAST PRU		
		NS	S		NS	S
NAVR	9	0.78 ± 0.68	73.83 ± 92.43	D1	0.14 ± 0.05	0.23 ± 0.10
				H1	0.19 ± 0.07	0.17 ± 0.11
PAVR (house dust, mites)	12	11.15 ± 9.92	551.45 ± 481.43	D1	1.81 ± 2.90	21.03 ± 22.42
				H1	0.64 ± 0.59	10.74 ± 13.13
SAVR (grass pollen)	4	44.08 ± 45.43	737.33 ± 941.50	G3	10.56 ± 15.06	35.5 ± 9.61

NAVR: Non allergic vasomotor rhinitis
PAVR : Perennial allergic vasomotor rhinitis
SAVR : Seasonal allergic vasomotor rhinitis

(non allergic vasomotor rhinitis, perennial allergic vasomotor rhinitis, seasonal vasomotor allergic rhinitis) and also from one group to another.

DISCUSSION

Criticism of the technic used for collection of nasal secretions and IgE determination

The use of nasal secretions in their native form constitutes a simple and easily performed procedure. For one thing, it helps avoid certain errors linked to the technical complexity, the repeated manipulations and the problems of dilution of certain other methods: use of filter paper (Lorin et al., 1972; Mygind and Thomsen, 1976; Mygind et al., 1975) and particularly nasal washout (Deuschl and Johansson, 1977; Merret et al., 1976). The risk of error is increased by the physicochemical caracteristics of the normal variations of nasal secretions in the course of a 24 hour period and of those variations encountered from one individual to another and from one disease to another (Lorin et al., 1972; Mygind, 1979; Yunginger et al., 1973). Only Okuda's technic (Okuda, 1975) is similar to ours although he used a 1/1 dilution of the nasal secretions.

The technic used for homogenizing the nasal secretions seems able to reduce to a minimum any risk of error in measuring any IgE possibly combined non specifically with nasal mucus and the disk paper or with possible trapping of IgE by the nasal mucin. The results of the measurements of specific IgE carried out on the same sample of nasal secretions but at different times seemed to confirm the feasability and reliability of the method. This technic appears simpler and less restrictive than ultra-centrifugation or ultrafiltration. In fact, this latter method required a greater quantity of nasal secretions of which a portion is "trapped" in the milliporous filter. A 1/1 dilution would seem to be an attractive technical expedient but it would necessitate a readjustment of the results. Furthermore these same results would only be accurate in a certain area of the reference curve which itself cannot be reliably determined.

The quantitative determination of the albumin in the nasal secretions would seem preferable to that of the total proteins which are made up of a complicated heterogenous mixture of numerous proteins.

Diagnostic usefulness

There is a good concordance between serum and local IgE (Table 4 and Figures 1, 2, 3) but the diagnostic usefulness of the quantitative determinations of total and specific IgE done on the nasal secretions is not evident. In fact measurements of IgE in the nasal secretions did not provide us with any important supplementary arguments in the group of nine subjects where it was impossible to establish with any certainty an allergic cause.

It appears that the minimum positive limit of specific IgE should not be set at 0.1

Table 4. Correlations between the different quantitative determinations for perennial allergic vasomotor rhinitis (PAVR) in nasal secretions (NS) and serum (S).

PAVR: IgA (mg/l) IgE (UI/ml) RAST (PRU) alb. (g/l)		case	coefficient of correlation	signification against zero 0.05	NS or S
IgA (NS)	IgA (S)	7	0.2659	0.7067	NS
IgE (NS)	IgE (S)	13	0.6354	0.5324	S
RAST (NS)	RAST (S)	12	D1 0.5291	0.5529	NS
			H1 0.4500		NS
IgE (NS)	alb. (NS)	11	0.1139	0.5760	NS
RAST (NS)	alb. (NS)	11	D1 0.0957	0.5760	NS
			H1 0.0490		NS
IgE (NS) / IgE (S)	alb. (NS)	10	0.0389	0.6021	NS
RAST (NS) / RAST (S)	alb. (NS)	11	D1 0.0077	0.5760	NS
			H1 0.0748		NS
IgE (S)	RAST (S)	11	D1 0.6618	0.5760	S
			H1 0.7509		S
IgE (NS)	RAST (NS)	12	D1 0.7933	0.5529	S
			H1 0.5559		S

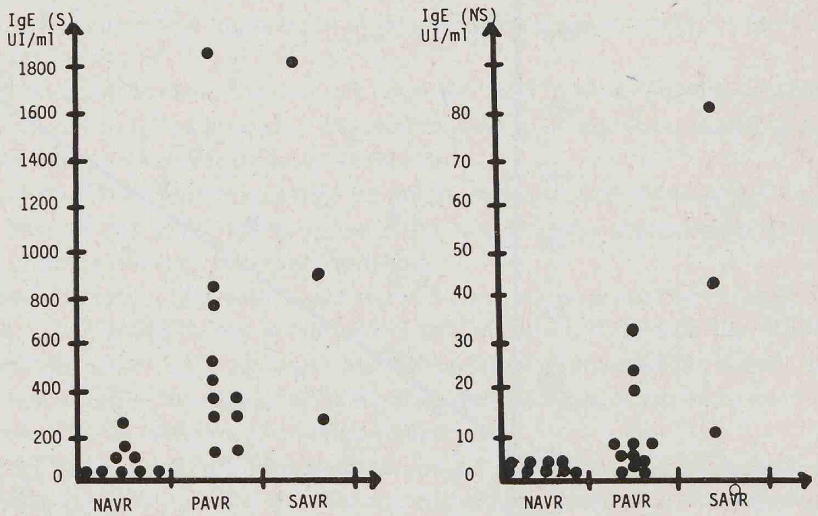


Figure 1. Serum IgE and local IgE in the different types of vasomotor rhinitis.

Figure 2. Local and serum specific IgE.

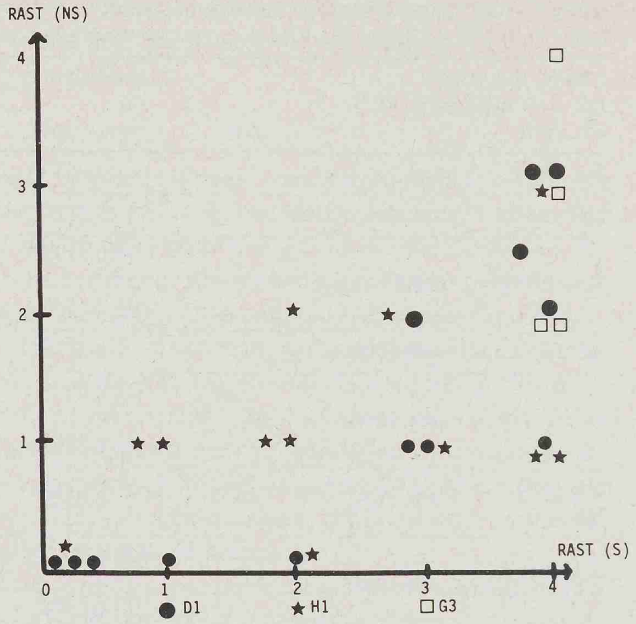
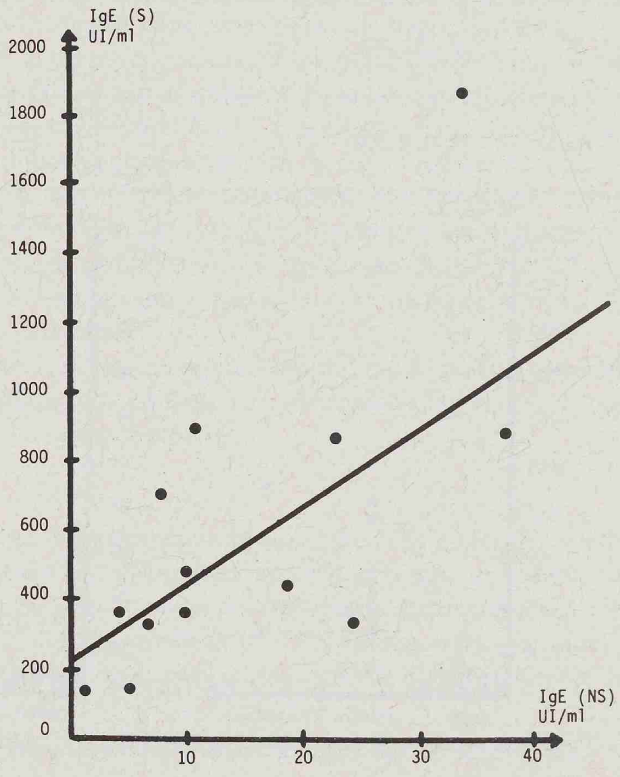


Figure 3. Correlation between serum IgE and Local IgE. (List square regression line).



or 0.2 PRU as had been recommanded by certain authors (Deuschl and Johansson, 1977; Nalebuff, 1978) whether these determinations were carried out on the serum or on nasal secretions.

In fact in seven of our control subjects, we have also found levels above 0.2 PRU in 7 out of 21 measurements (1 RAST D1: class 2; 1 RAST D1: class 1 and 1 RAST G3: class 1), and above 0.1 PRU in 14 out of 21 measurements done on nasal secretions for the different allergens (D1: 0.28 ± 0.45; H1: 0.17 ± 0.09; G3: 0.22 ± 0.11 in PRU). All of the nine patients with non allergic rhinitis had specific IgE levels above 0.2 PRU in the serum and/or in the nasal secretions, both for Dermatophagoides and dust allergens as well as for grass pollen allergens (Tables 1, 2, 3).

Correlations between the different parameters observed

In our group of patients the albumin level varies between 0.05 g/l and 2.25 g/l. This can be interpreted as a reflection of plasma transsudation because albumin cannot be synthesized in the nasal mucosa. For this reason, certain authors consider this as a standard of reference for the possible exchanges of IgE between the nasal secretions and the serum. However, certain reservations have to be kept in mind (Lorin et al., 1972; Mygind, 1979):

- the difference in molecular weight between albumin (69,000) and IgE (196,000);
- the variation of the level of albumin in any 24 hour period and from one individual to another;
- the complex regulation of the "vascular permeability" in the context of the vasomotor function of the pituitary;
- the frequency and importance of inflammatory phenomena in the nasal mucosa.

The albumin levels in the controls are lower than in those patients with vasomotor rhinitis (allergic or not). This would seem to be due to increased vascular permeability whatever its cause (Table 2).

Likewise it is difficult to quantify the IgE in the nasal secretions and to compare its level to that of IgE in the serum in the same subject much less to compare these levels between different individuals.

Measurements of IgE in the blood and in the secretions in relation to ml of "dilution space" could hardly be compared to each other. If, in fact, the "dilution space" for serum IgE is relatively homogenous and well known, it's not the same for that of IgE in the nasal secretions. The relationship between these two "dilution spaces" is complex and poorly understood.

As for specific IgE its measurement can be considered as semi-quantitative when carried out on pure secretions; it can only be qualitative if carried out on diluted nasal secretions.

In all of our cases, the level of total IgE (UI/ml) and of specific IgE (PRU or class of RAST) for dust allergens, mites, animal dander and to a lesser degree for grass pollen is lower in nasal secretions than in the serum as shown in Table 3. In our patient series, we were unable to find any statistically significant correlation either between total or specific IgE and the level of albumin in nasal secretions, or between the "weighted" levels of total local IgE and local specific IgE (relationship of total local IgE to total serum IgE and of local specific IgE to serum specific IgE) and the albumin in nasal secretions (Table 4).

On the other hand, there is statistically significant correlation between:

- total local and serum IgE (Figure 3, Table 4);
- total local IgE and local specific IgE (Table 4);
- total serum IgE and specific serum IgE (Table 4).

We did not find any correlation between local and specific IgE and between local and serum IgA (Figure 2, Table 4).

Criticism of concept of "localized allergy"

The interpretation of these results must likewise take into account the problable topographical heterogeneity of the sites of IgE synthesis. The results of the quantitative determinations we have carried out in cases of allergic rhinitis do not prove that the specific IgE (dust, dermatophagoides, grass-pollen) measured in the nasal secretions or in the serum are either exclusively or mainly nasal in origin. The levels of specific IgE are seemingly the expression of the sum of specific IgE for a given allergen synthesized by IgE secreting cells in the target organ - the nose in our case - and possibly by IgE secreting cells situated at other sites in other organs (bronchi . . .).

Our results may lead us to suspect a local synthesis of IgE in the target organ but would not allow us to attribute to it any role in a possible "local allergy". This latter concept has been proposed by certain authors in case reports of rhinitis with negative skin tests and/or absence of serum specific IgE (Huggins and Brostoff, 1975; Merret et al., 1976). Likewise the study of vasomotor rhinitis considered to be non allergic in origin do not give any further support to the notion of an "exclusively local allergy".

The comparative study of relationships, such as that of specific IgE in nasal secretions to total IgE in nasal secretions as compared to the relationship of specific IgE in the serum to total IgE in the serum, shows a greater proportion of specific IgE in relation to total IgE in nasal secretions than in the serum. Thus for Dermatophagoides there are proportionally about four times more specific IgE in relation to total IgE in the nasal secretions than in the serum. The local synthesis of IgE with possible preferential excretion into nasal secretions rather than into the serum could be a possible explanation. These data as well as the increase in local vascular permeability seem to point to a type of functional polarity. However, it

should be noted that the two "dilution spaces" of IgE are very different from each other and that the relationship between the two of them is poorly understood.

CONCLUSION

Despite numerous problems in methodology, quantitative determinations of IgE in nasal secretions could only confirm the clinical data and results of quantitative measurements in the serum. They provide no really new information concerning the diagnostic etiology of perennial vasomotor rhinitis where allergy represents only one of the many possible causes. Such an etiology is often a multifactorial determination capable of associating extrinsic factors such as allergy with intrinsic ones involving the neuro-vegetative system.

Moreover, they do not furnish any formal arguments in favor of a "local allergy" in the target organ. This is because of the many problems involved in the interpretation of the results of certain quantitative determinations within the framework of such a technic of investigation.

RÉSUMÉ

L'étude porte sur 32 sujets dont 7 témoins et 25 malades présentant une rhinite vasomotrice isolée, sans asthme associé. Parmi les 25 malades, 4 sont atteints d'une rhinite périodique et 21 d'une rhinite apériodique dont 12 relèvent d'une étiologie allergique certaine.

Les sécrétions nasales prélevées en même temps que le sérum, sont recueillies pures, non diluées sous contrôle rhinoscopique et après stimulation locale à la carbacholine. Différents dosages ont été pratiqués (albumine, IgE totales, IgE spécifiques, IgA) pour tenter d'évaluer leur intérêt dans le diagnostic étiologique de ces rhinopathies vasomotrices et dans le cadre du concept "d'allergie localisée à l'organe cible".

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